Outbreak of *Salmonella* Enteritidis linked to the consumption of frozen beefburgers received from a food bank and originating from Poland: northern France, December 2014 to April 2015

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A prolonged outbreak of *Salmonella enterica* serotype Enteritidis occurred in northern France between December 2014 and April 2015. Epidemiological investigations following the initial notification on 30 December 2014 of five cases of salmonellosis (two confirmed *S.* Enteritidis) in young children residing in the Somme department revealed that all cases frequented the same food bank A. Further epidemiological, microbiological and food trace-back investigations indicated frozen beefburgers as the source of the outbreak and the suspected lot originating from Poland was recalled on 22 January 2015. On 2 March 2015 a second notification of *S.* Enteritidis cases in the Somme reinitiated investigations that confirmed a link with food bank A and with consumption of frozen beefburgers from the same Polish producer. In the face of a possible persistent source of contamination, all frozen beefburgers distributed by food bank A and from the same origin were blocked on 3 March 2015. Microbiological analyses confirmed contamination by *S.* Enteritidis of frozen beefburgers from a second lot remaining in cases' homes. A second recall was initiated on 6 March 2015 and all frozen beefburgers from the Polish producer remain blocked after analyses identified additional contaminated lots over several months of production.

Introduction

While targeted control measures implemented in food production in France in the 1990s, notably in poultry, cattle and milk production, were shown to reduce the number of human *Salmonella* cases, *Salmonella* remains an important source of food-borne outbreaks in France [1]. In France, notification of food-borne disease outbreaks (FBDO) to the regional health agency (ARS) is mandatory for health professionals, clinical microbiologists and institutional catering services. Notifications can be made by telephone, email or fax using a standardised notification form. The ARS is responsible for case investigations while the Departmental Direction for the Protection of Populations (DDPP) is responsible for food safety investigations. The ARS then transmits the results of the outbreak investigations to Santé publique France (SpFrance), the French public health agency, which is responsible for epidemiological surveillance of FBDOs. In 2012, the notification rate for confirmed *Salmonella* cases in France was 13.3 per 100 000 population [2].

In addition to mandatory notification of FBDOs, private and hospital laboratories send *Salmonella* isolates on a voluntary basis to the dedicated French National Reference Centre (NRC) for serotyping and microbiological surveillance. In 2014, of 9,077 isolates received and analysed at the NRC, *Salmonella enterica* serotype Enteritidis (*S.* Enteritidis) was the third most frequently isolated serotype behind *S.* Typhimurium and monophasic variant 1,4,[5],12:i:- [3]. The same year, 1,380 food-borne outbreaks were notified to SpFrance, with *Salmonella* spp. representing the most common source in outbreaks with confirmed aetiology (110 of 254 FBDO (43%)) [4]. A recent study of the community incidence of salmonellosis in France from 2008 to 2013 estimated an annual community incidence rate of 307 cases per 100 000 population and 4,305 hospitalisations annually [5].

French departments of residence for identified confirmed, possible and probable cases of *Salmonella enteritidis*, northern France, December 2014 to April 2015
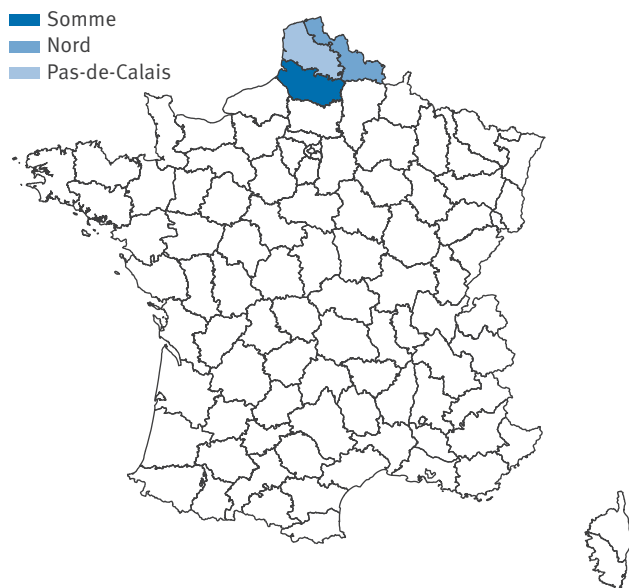
The event

In December 2014, the ARS in Picardy was notified by a hospital laboratory of five cases of salmonellosis in young children residing in the Somme department in a single week, of which two were confirmed *S.* Enteritidis and three were *Salmonella* spp. The number of cases was unusual for the laboratory, which typically observes one to two cases of *Salmonella* isolated in young children for the same time period. Preliminary investigations were initiated by the Santé publique France Picardy regional office using a standardised *Salmonella* questionnaire to identify food items and place of consumption or purchase. All cases, or a guardian for minors, were interviewed and a single common link with the consumption of food products from food bank A was identified. Further investigations were undertaken to identify the source of infection and implement appropriate control measures. Here we present the results from the prolonged outbreak of *S.* Enteritidis occurring from December 2014 to April 2015.

Methods

Outbreak investigations

We defined a confirmed case as a person residing in the Somme, Nord or Pas-de-Calais department with laboratory-confirmed infection of *S.* Enteritidis after week 51 2014. A probable case was a person residing in the Somme, Nord or Pas-de-Calais department presenting symptoms compatible with *Salmonella* infection (abdominal pain, diarrhoea, with or without recorded fever), and an epidemiological link to a confirmed case, after week 51 2014. A possible case was defined as a person residing in the Somme, Nord or Pas-de-Calais department presenting symptoms compatible with

Salmonella infection (abdominal pain, diarrhoea, with or without recorded fever), but no laboratory confirmation, after week 51 2014. Human-to-human transmission was suspected for cases presenting symptoms › 7 days after incident cases.

Cases were identified from three sources: (i) an active search of cases from private laboratories in the cities where initial cases were identified (two cities in the Somme department) and identification of cases in the families of incident cases representing outbreak clusters; (ii) mandatory notification of food-borne disease outbreaks occurring in northern France; (iii) microbiological surveillance data from the NRC of all confirmed cases sent by laboratories in the department were cases had been notified since week 51 2014. In parallel, the NRC also verified that no other French departments had presented an unusual number of cases of *S.* Enteritidis for the same time period. Cases, or a guardian for minors, were asked about their food consumption in the week before symptom onset using a standardised *Salmonella* questionnaire administered by telephone between 30 December 2014 and 22 April 2015. Information was collected on at risk activities (travel abroad, contact with animals) as well as food items consumed and the place of purchase of all food items.

Microbiological and food trace-back investigations

In France, human *Salmonella* isolates received at the NRC are analysed using the White-Kauffmann-Le Minor scheme for serotyping and standardised multilocus variable tandem repeat analysis (MLVA) for comparison of cases in the context of outbreak investigations [6,7]. Food isolates were analysed by the Laboratory for Food Safety of the French Agency for Food, Environmental and Occupational Health and Safety (ANSES) using serotyping by agglutination followed by MLVA for *S.* Enteritidis, which is common practice in the case of food-borne outbreak investigations [7].

When available, *Salmonella* spp. isolates from notified cases were sent to the NRC for serotyping. Available food samples were collected for microbiological testing by the Laboratory for Food Safety of the ANSES. Ten human and food sample strains each were analysed by MLVA to confirm the microbiological link.

Food trace-back investigations were conducted by the DDPP in the Picardy region and by the General Directorate for Food (DGAL) for national and international investigations.

European investigations

European health authorities were notified about the outbreak and of the suspected source of contamination via the European Commission's Early Warning and Response System (EWRS), the European Epidemic Intelligence Information System platform (EPIS) run by the European Centre for Disease Prevention and

Possible, probable and confirmed cases of *Salmonella Enteritidis,* by week of symptom onset, northern France, December 2014 to April 2015 (n=71)
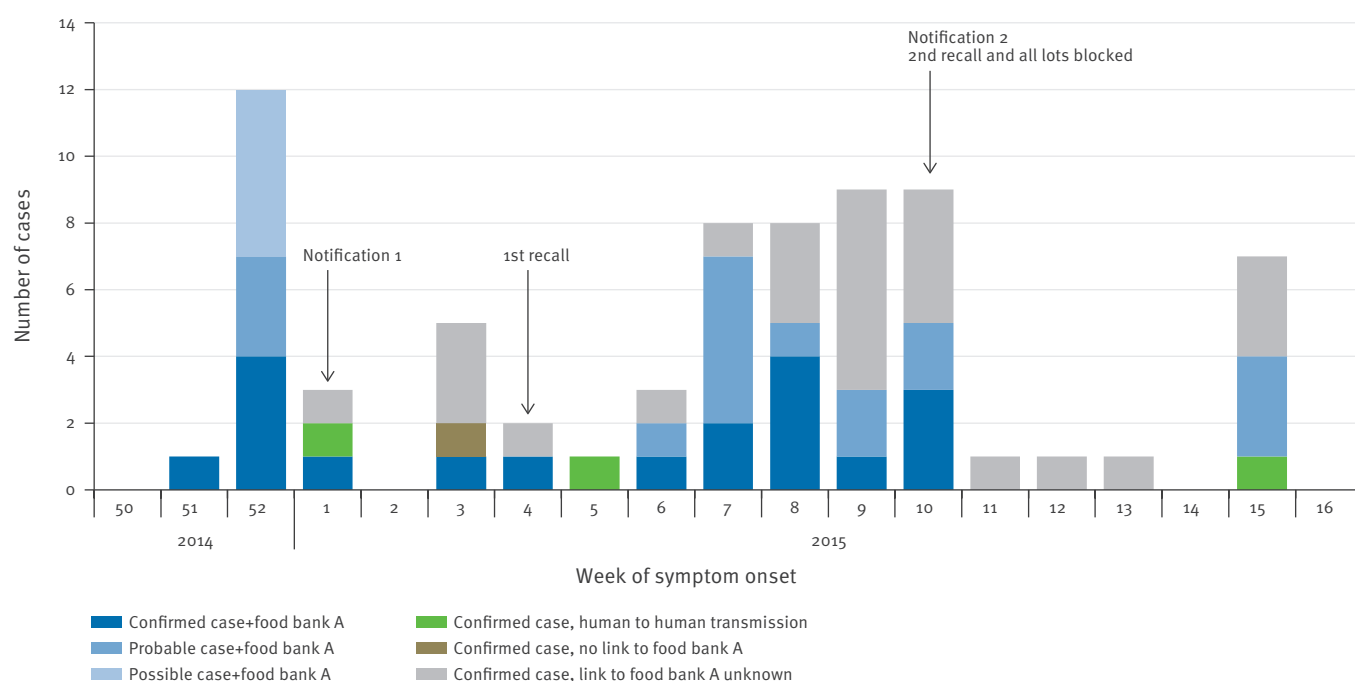
For 28 cases with information on date of symptom onset missing, the date of strain isolation was used.

Results

Epidemiological investigations

A total of 45 cases identified from notifications by hospitals, medical laboratories, mandatory notification of FBDOs, and the NRC listing, were interviewed regarding their food consumption. Twenty-three were confirmed *S.* Enteritidis, 17 were probable cases and five were possible cases. An additional 26 confirmed cases identified only from the NRC listing were not interviewed either because they could not be contacted (four cases) or because the information was available only after implementation of outbreak control measures which took place on 22 January and 3 March 2015 (22 cases). These cases were not contacted because they occurred up to several weeks before control measures and the aim of investigations at this stage of the outbreak was to identify cases occurring after control measures in order to verify their efficacy.

The first outbreak notification occurred on 30 December 2014 and the second on 2 March 2015. All 45 interviewed cases resided in adjacent departments in northern France: 37 cases in the Somme department, six cases in the Nord department and two cases in the Pas-de-Calais department (Figure 1). Information on age was known for 37 of 45 cases and ranged from 1 month to 49 years old (median age: 9 years). The male to female sex ratio was 1.1 (information available for 40 of 45 cases). In total eight children and one adult were hospitalised.

Of the 45 cases with food consumption information, 41 had consumed frozen beefburgers from food bank A and no other common source of infection was identified. Of the four remaining cases, three were human-to-human transmission with incident cases reporting consumption of frozen beefburgers from food bank A and one case reported no link with food bank A and no consumption of frozen beefburgers. In nine families (14 cases) specifying mode of cooking of the frozen beefburgers, only three (six cases) reported consuming the beefburgers well-done (no pink visible). A total of 11 FBDOs were identified, one by mandatory notification and ten during investigations of cases.

Symptom onset ranged from 21 December 2014 to 6 April 2015. The outbreak curve shows two outbreak waves (Figure 2). Four cases notified in week 15 2015 occurred in the same family, who reported regularly storing frozen beefburgers from food bank A for several weeks in their freezer.

Microbiological and food trace-back investigations

Following the initial notification and epidemiological investigations identifying a common link with food bank A, food trace-back investigations were initiated

Control, and the European Commission's Rapid Alert System for Food and Feed (RASFF).

FIGURE 3

Schema showing the distribution network of frozen beefburgers originating in Poland and distributed by food bank A in northern France, December 2014 to April 2015
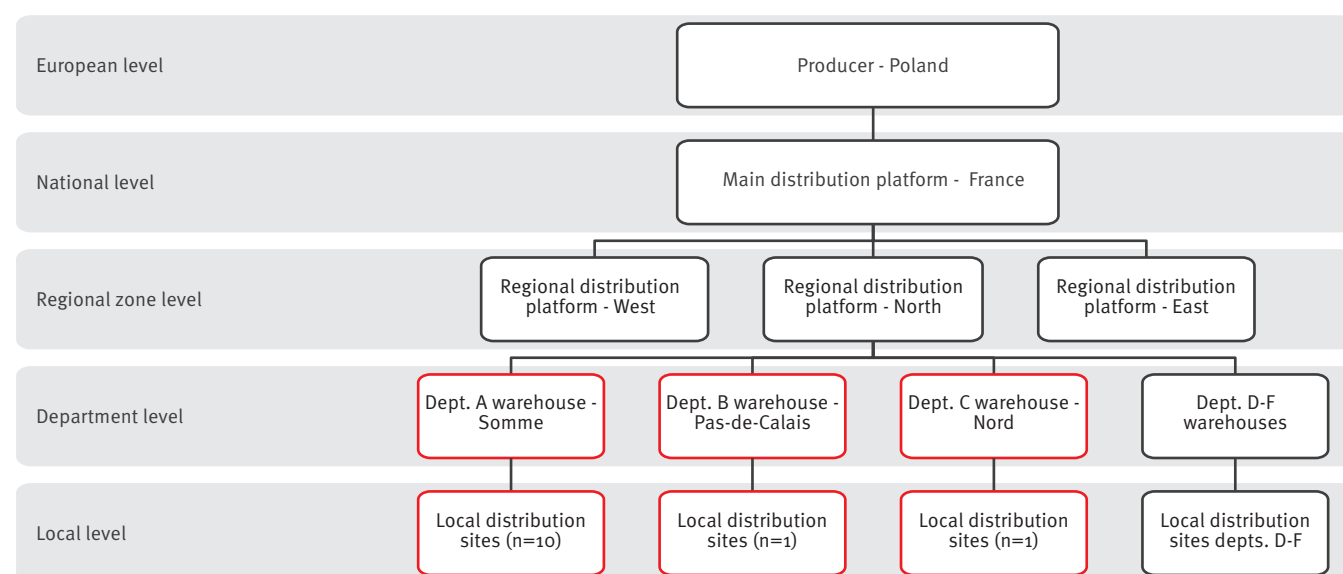
Dept: department.

Red boxes show the warehouses and local distribution sites at department level where the lots of beefburgers linked to confirmed, probable or possible Salmonella Enteritidis cases were identified.

on 8 January 2015. The geographic distribution of the cases suggested a food source contaminated before distribution as cases frequented food bank A at different local distribution sites (10 sites in the Somme, one in the Nord and one in the Pas-de-Calais). While a total of six departments received frozen beefburgers from the suspected lot, cases were only identified in three departments (Figure 3). Visits to three local sites of food bank A as well as the regional distribution platform for northern France by the DDPP revealed no non-compliance in storage conditions or respect of the cold chain.

As of 9 January 2015, food bank A temporarily blocked the distribution of all lots of frozen beefburgers. Based on the dates and locations of food bank A sites frequented by the cases, a common lot of frozen beefburgers from a producer in Poland was identified, lot A, distributed from December onward. A recall of lot A was initiated on 22 January 2015. No other French commercial or charitable groups received frozen beefburgers of the same lot from the Polish producer. No food samples of lot A from case homes were available for testing. However, international food trace-back investigations revealed that two samples from lot A tested positive in August 2014 for *Salmonella* spp. by the Polish producer in the context of controls requested by the specifications of the public contract with food bank A. After removal of the concerned part of the lot, a second series of samples in September 2014

tested negative and the lot was sent by the producer to France for distribution. For the other lots blocked by food bank A, no other elements (positive test results, human cases or information from Polish authorities) were known and they were put on the market with the authorisation of the DGAL.

Epidemiological investigations demonstrated that several cases identified after the second notification on 2 March 2015 began frequenting food bank A in February 2015, after the first recall, indicating that a second contaminated lot was in distribution. Frozen beefburgers from three different lots (B, C, D) were available for analysis in the homes of three cases. All of the available burgers were sampled two to three times. Analysis of 14 samples in six burgers from lot B yielded 12 positive results for *S.* Enteritidis. Seven samples from three burgers from lots C and D were negative.

All lots from the Polish producer were blocked as of 3 March 2015 and a recall of lot B was initiated on 6 March 2015. The rest of the lots remained blocked in France from distribution pending information from the Polish authorities regarding adherence to good hygiene practices (GHP) and Hazard Analysis Critical Control Point (HACCP)-based procedures by the Polish producer. This information was necessary to determine action regarding the remaining batch: further analyses, destruction, heat treatment, or return to the Polish producer.

Comparison by MLVA of 10 *Salmonella* strains identified in the human cases and 10 food samples showed the same profile 2_10_7_3_2 (VNTR loci order: SENTR7 SENTR5 SENTR6 SENTR4 SE3), confirming the link between cases from the entire outbreak period and with the contaminated frozen beefburgers from lot B (implicated in the second wave of the outbreak).

In both outbreak waves, the suspected lots of frozen beefburgers were distributed in several French departments in northern France; however, the majority of cases identified as having a link with food bank A were in the Somme department. Additional food trace-back investigations aimed to identify a potential explanation for the geographic distribution of cases (storage or distribution conditions at the local level, problems with the cold chain), but no such problems were identified. Analysis of NRC data did not identify any other French departments with an excess in cases of *S*. Enteritidis and no other region reported food-borne outbreaks citing food bank A or frozen beefburgers as the suspected source.

European investigations
European health authorities were notified of outbreak investigations and the suspected link with frozen beefburgers from the Polish producer through a message on the EWRS on 10 March 2015. Messages to European epidemiologists and microbiologists were sent through the EPIS platform on 12 March 2015 sharing results of epidemiological and microbiological investigations. No other countries reported outbreaks of *S*. Enteritidis linked to consumption of frozen beefburgers from the Polish producer.

An alert was sent on the RASFF on 6 February 2015 (2015.0137) and a second one on 10 March 2015 (2015.0293) following the second outbreak. Through the RASFF, information obtained from Polish authorities did not indicate a failure to respect good hygiene practices by the Polish producer.

Discussion and conclusion
Food-borne disease outbreaks due to *Salmonella* in France have been described in a variety of different food items including dried sausages, raw milk cheese and infant formula [8-11]. In 2010 an outbreak of *S*. Typhimurium linked to the consumption of beefburgers from Italy occurred in four schools in Poitiers, France, with over 550 confirmed cases [12]. While *S*. Enteritidis is typically associated with poultry and poultry products in France and elsewhere in the European Union [13,14] other food products may be the source of contamination. Most recently in 2014, a large outbreak of *S*. Enteritidis (displaying a different MLVA type) in the Hautes-Pyrénées department in the south of France was linked to the consumption of raw milk cheese with 181 confirmed and suspected cases identified (unpublished data). In the present outbreak, microbiological investigations confirmed the presence of *S*. Enteritidis in frozen beefburgers consumed by

cases, corroborating the results of the epidemiological investigation.

The geographic distribution of cases primarily in the Somme department could be explained by several hypotheses. Regarding epidemiological investigations, several factors may contribute including (i) the population base for the department hospitals (a single large university hospital with paediatric emergency services in the Somme) may have centralised more cases than in other departments, leading to notification by the hospital; (ii) the occurrence of the outbreak in the winter during a period of increased cases of viral gastroenteritis which may have further decreased the likelihood that doctors prescribed stool analysis except in severe cases; and (iii) the exhaustiveness of food-borne outbreak surveillance in France.

Notably, the human *Salmonella* surveillance system is based on analysis at the NRC of *Salmonella* isolates sent on a voluntary basis by hospital and private laboratories, which is complemented by the mandatory notification of FBDOs. The exhaustiveness of these two complementary systems is estimated at 66% and 26% respectively [3,13]. While 11 FBDOs were identified among the cases, only one was notified to regional health authorities. The remaining 10 were identified through epidemiological investigations of confirmed cases notified by the hospital laboratory or the NRC. An excess of cases would likely have been detected by the weekly alert algorithm run at the NRC, but as the median delay from sample isolation to serotyping results is 14 days [15], the alert would have occurred several weeks into the outbreak. In this instance, the reactivity of hospital laboratory in notifying initial cases allowed for more timely epidemiological investigations and appropriate control measures.

Another possible explanation for the geographic distribution of cases, regarding food trace-back and microbiological investigations, is that the contamination was not homogenous, but concerned one or a few mixes (each lot was constituted of different mixes of ground beefprocessed over a given production period) in portions of the lots that were distributed primarily in the Somme department.

The described outbreak is unique in that it affected a specific population of individuals frequenting food bank A. A review of the literature regarding food-borne outbreaks did not return any articles regarding outbreaks linked to food distributed by food banks. Initial epidemiological investigations identifying a common link with food bank A for all families of confirmed cases was unusual and allowed for a more rapid orientation of epidemiological and food trace-back investigations after confirming the absence of other links between cases (commercial supermarkets, local markets).

This outbreak was also characterised by a large number of familial FBDOs identified during epidemiological

investigations of confirmed cases, especially in the second wave. In the first outbreak wave, three FBDOs were identified in the families of 16 incident cases. In the second wave of the outbreak, eight families of 25 incident cases reported FBDOs. Furthermore, two-thirds of families reporting degree of doneness indicated that the burgers were consumed medium-rare or rare. Although it was not possible to quantify contamination levels, this could indicate that the frozen beefburgers were highly contaminated and that contamination levels may have been greater for the second lot recalled (lot B) based on the greater number of family FBDOs around incident cases.

The source of the outbreak was identified through epidemiological, microbiological and food trace-back investigations as frozen beefburgers originating from Poland. Large scale FBDOs requiring international trace-back investigation have been described for a wide variety of pathogens and food products [16-18]. Specifically, *Salmonella* outbreaks in European countries traced to imported food products have been previously reported, most recently *S*. Enteritidis linked to eggs from a German producer [19,20].

Such outbreaks can present difficulties related to the food trace-back investigations and control measures because numerous countries are implicated. This makes exchanges with different food safety authorities necessary to obtain information useful for the management of the outbreak such as information regarding hygiene practices by the producer, previous microbiological analyses in country of origin and return of remaining product. In this outbreak, the specificity of the food distribution chain for food banks presented challenges for food trace-back and management of remaining product. The frozen beefburgers were obtained through bids by producers for the Fund for European Aid to the Most Deprived (FEAD) and there is no commercial relationship between the food banks receiving products and the Polish producer. Analyses of the remaining lots based on a sampling plan established by the ANSES identified additional contaminated lots covering a production period of several months.

Overall, it is probable that the 44 cases with a confirmed link to food bank A in this outbreak represent just a small proportion of the actual number of cases that occurred in connection with the consumption of frozen beefburgers from food bank A. This outbreak highlights the important role of medical and laboratory personnel in the notification of unusual disease events that complements existing surveillance systems. The reporting of an unusual number of cases of salmonellosis in young children by a single hospital laboratory allowed for a rapid public health response that identified an unusual epidemiological link between the cases. Consequently, both national and international food trace-back investigations proceeded quickly, with timely information to European Union Member States that confirmed the absence of widespread distribution of the contaminated product, and led to a recall of contaminated lots and appropriate public health measures to ensure the safety of the remaining product.

Conflict of interest

None declared.

Authors' contributions

Epidemiological investigations were conducted by GJ and CV and coordinated by NF and NJ. SLH and SCS coordinated human and food microbiological investigations. Food trace-back investigations were coordinated by NP. GJ drafted the manuscript and all authors contributed editing and to final approval of the manuscript.

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Tuberculosis contact investigations associated with air travel in Ireland, September 2011 to November 2014

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The risk of communicable disease transmission during air travel is of public health concern and has received much attention over the years. We retrospectively reviewed information from nine flights (≥8 hours) associated with infectious tuberculosis (TB) cases in Ireland between September 2011 and November 2014 to investigate whether possible transmission had occurred. Twenty-four flights notified in Ireland associated with sputum smear-positive pulmonary TB cases with a history of air travel were reviewed. Nine were suitable for inclusion and analysed. Six cases of infectious TB travelled on nine flights. A total of 232 passengers were identified for contact tracing; 85.3% (n = 198) had sufficient information available for follow-up. In total, 12.1% (n = 24) were reported as screened for TB. The results revealed no active TB cases among passengers and 16.7% (n = 4) were diagnosed with latent TB infection (LTBI) all of whom had other risk factors. Despite the limited sample size, we found no evidence of *M. tuberculosis* transmission from infectious passengers. This study identified challenges in obtaining complete timely airline manifests, leading to inadequate passenger information for follow-up. Receipt of TB screening results from international colleagues was also problematic. The challenge of interpreting the tuberculin skin test results in determining recent vs earlier infection was encountered.

Introduction

Tuberculosis (TB) remains a significant cause of mortality and morbidity with an estimated 9.6 million new TB cases reported worldwide each year [1]. Drug resistance is also a major challenge with 3.3% of new TB cases and 20% of previously treated cases having multidrug-resistant TB (MDR-TB) globally [1]. Although great progress has been made in the control of TB in recent years, it remains a public health concern in most countries in the World Health Organization (WHO) European Region with an estimated 360,000 incident TB cases occurring during 2013 [2]. The absolute number of incident TB cases fell by 20,000 in 2013, corresponding to a 5.6% decline compared with the previous year in Europe [2].

In Ireland the incidence of TB has been declining. Over the past 10 years, the number of TB cases notified decreased from 450 in 2005 to 318 cases in 2014 [3]. As TB remains a serious global public health issue, many interventions are aimed at preventing and controlling disease transmission nationally and internationally. Contact tracing is one of the key measures in the management and control of TB as early detection of new cases reduces the timeframe during which a person is infectious.

Many studies have been conducted to investigate the possibility of TB transmission during air travel. The Centers for Disease Control and Prevention (CDC) in the United States (US) conducted six investigations between 1992 and 1995 examining the possible transmission of TB during air travel [4]. Only two of these investigations reported evidence of possible TB transmission [5,6]. Other studies, including an extensive systematic review conducted in the United Kingdom (UK), found the risk of transmission to be low or inconclusive [7-13].

The length of contact necessary for TB infection to be transmitted is variable and depends on a number of factors including the infectiousness of the index case, the susceptibility of the individual exposed and the environment where the exposure occurred [14]. Guidelines published by WHO on TB and air travel [15] state that the risk of possible TB disease transmission during air travel is associated with sitting within two rows of an infectious passenger on flights lasting 8 hours or longer. The guidelines also recommend contact tracing be conducted within the 3-month period between date of travel and date of notification. Given the difficulties in assessing infectiousness at the time of the flight, interpreting tuberculin skin test (TST) results to determine recent vs earlier infection and obtaining sufficient accurate passenger travel and seating details,

3 months is considered the maximum time after travel that warrants public health intervention [15].

In Ireland, the 2010 guidelines on the prevention and control of tuberculosis [16] recommend contact tracing for passengers on board an aircraft who were exposed to a confirmed case of infectious TB as per the WHO guidelines. In this context, we decided to review information on all cases of infectious TB associated with air travel reported in Ireland between September 2011 and November 2014 to investigate the possibility of TB transmission.

Methods

All TB notification records were reviewed to identify cases with a history of air travel. Flights lasting less than 8 hours as well as flights where the 3-month period had elapsed between the date of the flight and the date of notification to public health authorities were excluded from the analysis. All cases of sputum smear-positive pulmonary TB with a history of air travel on flights of 8 hours or more duration in the 3 months before notification to the Health Protection Surveillance Centre (HPSC) in Ireland between September 2011 and November 2014 were retrospectively reviewed. The following outlines the steps taken during the investigation of flight contacts.

For each case notified to HPSC, data were collected on the index case from the notifying clinician on the site of disease, symptoms including onset date, treatment and microbiology results including drug sensitivities where available. Details of the relevant flights were obtained from regional public health departments. Following this, the relevant airline was contacted using a standardised letter and the passenger manifest requested as per national and WHO guidance on passenger contacts seated in the same row and two rows in front of and behind the index case in order to identify passengers requiring TB screening. Specific ethical approval was not required to undertake this study, as under the Irish Infectious Disease Regulations (1981) [17] follow-up of contacts of infectious cases of TB is required as part of routine work to prevent further spread of disease.

Where sufficient passenger contact information was available, this information was then sent to the relevant regional departments of public health in Ireland and internationally to the relevant national TB surveillance and control focal points and TB screening including results was requested on the contacts.

Data were analysed using case counts and frequencies.

Results

Between September 2011 and November 2014, a total of 24 commercial flights associated with infectious cases of TB were reported in Ireland. Contact investigation was carried out on nine of these flights. Fifteen flights were not followed up: for five of these the 3-month period had elapsed between the date of the flight and the date of notification; and the airline manifest was not provided by the airline for seven flights, despite frequent requests. The remaining three flights were less than 8 hours duration and therefore no further follow-up was required.

For the nine flights investigated, the median estimated duration of flights was 8 h 40 min (range: 8 h to 11 h 40 min; IQR: 8 h 20 min to 8 h 40 min). A total of six index cases (four male, two female; age range: 33–81 years) travelled on the nine flights. All cases were diagnosed as sputum smear-positive pulmonary TB and were deemed to be infectious at the time of travel. The quality of the data received from the airline manifest varied between flights and airlines. Four of the index cases were diagnosed with pan-sensitive strains of *Mycobacterium tuberculosis* and two index cases were diagnosed with *M. tuberculosis* resistant to isoniazid (Table).

Of the nine flights investigated a total of 232 passengers were identified for TB contact tracing. Of these identified passengers, 85.3% (n = 198) had sufficient personally identifiable information available from the airline manifest. No airline crew were included for contact tracing. The number of passengers requiring TB screening on each flight varied due to the type of aircraft and whether a bulkhead wall was situated within the five rows that were relevant for contact tracing.

Follow-up was made with local and international colleagues for TB screening results. Screening results were reported for six of the nine flights.

Where information requesting TB screening on passenger contacts was available, 10.6% (n = 21) were Irish citizens, and 89.4% (n = 177) were international contacts. Screening results were obtained on a total of 24 passenger contacts. Of these 24 passenger contacts with screening results obtained, 16 were screened in Ireland and eight were screened abroad. Two passenger contacts were identified as family members and deemed close contacts to one of the index cases; no other relationships were identified between the index cases and other passenger contacts.

Where TB screening results were available (n = 24) the type of test used for screening was available for 23 passengers. One passenger was clinically assessed for active TB and was from a country of high endemicity (≥40 cases of TB per 100,000 population per year).

Figure 1 below presents details of the type of test used for TB screening in the 23 passengers where information on type of screening test used was available. The majority of passenger contacts were screened using the tuberculin skin test (TST). Information on the size of the TST induration was not available for most of the passengers and results were reported as being positive or negative.

Tuberculosis screening test type used in contact investigations associated with air travel in Ireland, September 2011 to November 2014 (n = 23)
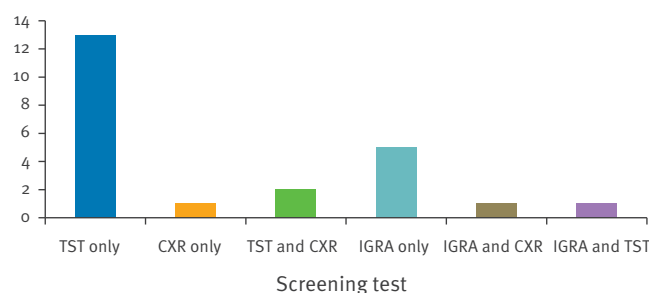
CXR: chest X-ray; IGRA: interferon-gamma release assay; TST: tuberculin skin test.

One passenger was clinically assessed for active TB only, was resident in a high-endemic country and is not presented in this figure.

A total of 13 passengers had only TST performed, five had interferon-gamma release assay (IGRA) test performed and two passengers had both TST and chest X-ray. One passenger was screened with both IGRA and TST as the TST reading was 14mm; however, confirmatory results of the IGRA were negative. This passenger contact also had a bacillus Calmette-Guérin (BCG) scar. One contact was screened using IGRA and chest X-ray and the remaining passenger was screened by chest X-ray only. The screening results are outlined in Figure 2.

Screening results

Where results were available (n = 24) no active cases of TB were identified. Four passenger contacts were diagnosed with latent TB infection (LTBI). All four had other risk factors for LTBI. Two had travelled with the index case and were from a country of high endemicity. However, despite this, it was not possible to exclude transmission before air travel. The remaining two passenger contacts were also from a country of high endemicity, of whom one was also a healthcare worker.

Discussion

This study investigated the possibility of *M. tuberculosis* transmission during air travel and found no evidence to support it. No active cases of TB were identified. Four passengers were diagnosed with LTBI; all were from countries of high-endemicity and one was a healthcare worker. In flight investigations it is often possible that passengers seated close to the index case may be family or friends. In this study, two passenger contacts diagnosed with LTBI had also travelled with the index case from a high-endemicity country and in this context it was not possible to determine whether transmission occurred during air travel or due to prior exposure. The inability of the TST to distinguish between recent vs earlier infection also contributes to this.

Results of tuberculosis screening by test type, contact investigations associated with air travel in Ireland, September 2011 to November 2014 (n = 23)
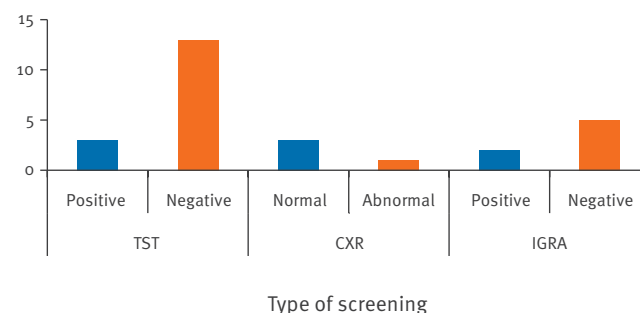
TST: Tuberculin skin test; CXR: chest X-ray; IGRA: interferon-gamma release assay.

One passenger was clinically assessed for active tuberculosis only and was resident in a high-endemicity country and is not presented in this figure.

Some passenger contacts had more than one type of screening test performed.

This study also identified challenges faced in obtaining complete timely airline manifests, which can lead to inadequate passenger information. Receipt of TB screening results from international colleagues was also challenging. Of all passenger contacts requiring TB screening, only 21 were identified as Irish citizens and 177 were international contacts. Of the 21 contacts screened in Ireland, results were received on 16, and of the 177 passenger contacts identified as international contacts, results were received on only eight contacts.

Interestingly, from published literature to date, no cases of active TB have been identified as a result of exposure to an infectious passenger during air travel and evidence suggests that few individuals infected with *M. tuberculosis* progress to active disease [18]. This study is consistent with previous contact investigations of TB during air travel, indicating that the risk of possible TB transmission is low. A large study conducted in 2010 in the US presented aggregated data from 131 index cases including 4,550 passenger contacts. This study identified that 182 (24%) had positive results and of the 142 passenger contacts with positive results for whom risk factor information was available, 130 (92%) had at least one risk factor and 12 (8%) had no risk factors. This study highlighted that positive TB test results were significantly associated with risk factors for prior TB [19]. This is reflected in our smaller study also.

A detailed UK systematic review [7] undertaken in 2010 reviewed 39 studies of which 13 were included in the review. This review found no evidence of transmission with only two studies reporting reliable evidence. The results also suggested reason to doubt the value of actively screening air passengers for infection with *M. tuberculosis* and recommended that the resources

TABLE

Tuberculosis contact investigations associated with air travel in Ireland, profile of index case, flight details, contact details and results, September 2011 to November 2014

Flight (n=9)	Date of flight	Infectivity and diagnosis of index case (n=6)	Age group (years) of index case at time of travel	Drug resistance	Number of potentially exposed passengers as per airline manifest[a]	Number of passengers with information available from airline manifest	Number of passengers with screening results available	Number of LTBI positives	Estimated duration of flight (h:min)	Interval (days) between date of flight and date of notification	Interval (days) between date of information request from airline and receipt of airline manifest
Dubai–Dublin	Nov 2014	Sputum smear-positive for *M. Tuberculosis*	50–59	Isoniazid	20	20	3[b]	0	8:20	41	3
Johannesburg–Dubai	Nov 2014				24	22	1[c]	0	8:00	42	3
Abu Dhabi–Dublin	Sep 2014	Sputum-smear positive for *M. Tuberculosis*	Unknown	No	15	6	2[d]	1	8:40	32	26
Rio de Janeiro–London	Sep 2013	Sputum smear-positive for *M. Tuberculosis*	30–39	Isoniazid	39	39	0	0	11:40	17	3
Abu Dhabi–Dublin	Jul 2013				27	18	6[e]	0	8:40	56	36
Johannesburg–Abu Dhabi	Jul 2013	Sputum smear-positive for *M. Tuberculosis*	40–45	No	10	7	0	0	8:20	23	36
Abu Dhabi–Johannesburg	Jun 2013				27	16	3[f]	0	8:40	55	36
Dubai–Dublin	Jul 2012	Sputum smear-positive for *M. Tuberculosis*	80–89	No	26	26	9[g]	3	8:15	9	2
Paris–Seoul.	Sep 2011	Sputum smear-positive for *M. Tuberculosis*	30–39	No	44	44	0	0	10:50	95	6
Total		NA	NA	NA	232	198 (85.3%)	24 (12.2%)	4 (16.6%)	NA	NA	NA
Median (interquartile range)		NA	NA	NA	NA	NA	NA	NA	8:40 (8:20–8:40)	41 (23–45)	6 (3–36)

CXR: chest X-ray; IGRA: interferon-gamma release assay; LTBI: latent tuberculosis infection; *M. tuberculosis*: *Mycobacterium tuberculosis*; NA: not applicable; TST: tuberculin skin test.

a Passengers seated in the same row and two rows in front of and behind the index case.

b One contact had TST and two contacts had IGRA only performed.

c One contact had TST only performed.

d IGRA performed on both contacts.

e Five contacts had TST only performed; one contact had TST and IGRA.

f Two contacts had TST only performed and one contact had was clinically assessed for active tuberculosis.

g Four contacts had TST only performed; one contact had a CXR only; two contacts had both a TST and CXR; one contact had an IGRA; one contact had an IGRA and CXR.

used might be better spent addressing other priorities in TB control.

Based on currently available evidence, the risk of TB transmission during air travel is very low. A recent systematic review estimates the risk of TB transmission from a sputum smear-positive index case during air travel to be 0.1–1.3% [20].

In Ireland, current guidelines for the prevention and control of TB recommend contact tracing passengers as per the WHO guidelines, i.e. limited to the same row as the index case and two rows in front of and behind the index case. However, the updated risk assessment guidelines for infectious diseases transmitted on aircrafts (RAGIDA) by the European Centre for Disease Prevention and Control (ECDC) in 2014 [21] recommend considering additional criteria before commencing contact tracing of passengers during air travel. They advise contact tracing be commenced if the index case is confirmed with infectious pulmonary TB, and if there is evidence of transmission in other settings, such as transmission to household members or other close contacts. These guidelines suggest that where these criteria are met, exposed passengers in the relevant rows of the aircraft be contacted using the procedure outlined in the WHO guidelines. These RAGIDA guidelines also point out that in instances where (despite extensive efforts) no information on evidence of transmission to close contacts can be obtained, the national authority can nevertheless decide to initiate contact tracing in these exceptional circumstances. Investigating contact passengers using the 2014 RAGIDA criteria, however, could pose a challenge as in some instances the interval between case notification and identification of close contacts may be longer than anticipated due to various reasons, e.g. delays in locating contacts or delays in contacts presenting for screening. In such instances the 3-month interval as recommended in national and international air flight guidance between case notification to public health and date of flight may have elapsed.

Based on the available evidence on TB transmission during air travel, the National Institute for Health and Care Excellence (NICE) in the UK recommends that following a diagnosis of TB in an aircraft passenger, contact tracing of fellow passengers should not routinely be undertaken. They recommend that the consultant in communicable disease control (CCDC) provides the airline with 'inform and advise' information to send to passengers seated in the same part of the aircraft as the index case [22].

Although there were limitations to this study, no cases of active TB were reported. This study was limited by the lack of comprehensive information from the airline manifests on each occasion. In total, 34 passengers had insufficient information available from the airline manifest and it was not possible to identify these passengers' country of origin for screening. This limited the comprehensive follow-up on each exposed contact. Other limitations included the fact that only nine flights were eligible for follow-up, therefore further limiting the conclusions drawn from the study as over half of flights reported were not followed up. The incomplete receipt of TB screening results from international and national colleagues also limited the findings of this study.

Although information was available and TB screening requested on 198 passenger contacts, not all of these had sufficient information available, with some passengers only having nationality and passport numbers available from the airline manifest. As a result of this paucity of information, we cannot be certain how many of these passenger contacts were followed up as we received no further communication. Therefore, it was not possible to assess the effectiveness of TB contact tracing in these passengers.

The challenges faced in communicating with airlines and international colleagues regarding public health threats and subsequent interventions were highlighted in this study. The importance of improving communication between airlines and public health in relation to public health threats in general and improving the quality and timeliness of the data provided by airlines must remain a priority. This is particularly important due to the continuous emergence of new viruses and increased globalisation.

This study clearly highlights the difficulties and challenges experienced with TB contact tracing due to the poor quality of passenger contact information. This is not unique to Ireland with similar findings identified in a UK study which highlighted that the process of tracing and investigating contacts of air passengers infectious with TB is usually unsuccessful without the availability of appropriate contact information from the airlines [23].

This study also identified the challenges faced by public health in following up and screening contacts both nationally and internationally. As screening results were only obtained for 24 passengers, the possibility of more widespread transmission cannot be excluded. Contact tracing is time consuming and requires extensive resources. Questions in relation to the value of contact tracing passengers exposed to infectious TB during air travel were raised from this investigation and in relation to the possibility of more effectively re-allocating resources to other TB preventive and control activities. Consequently we recommend reviewing current Irish national policy in terms of routine contact tracing of passengers exposed to TB infection during air travel and exploring whether we should adapt the UK approach as outlined in the 2011 NICE guidance in terms of providing 'inform and advise' information only to passengers who have been exposed to TB on long-haul flights.

Conclusion

Contact tracing has been used extensively in the prevention and control of TB. This retrospective review provided a unique opportunity to investigate the possibility of *M. tuberculosis* transmission during air travel. With an increase in flights to and from countries of high TB endemicity, the risk of passengers exposed to TB is inevitable, although our study found no evidence to support the transmission of *M. tuberculosis* from infectious passengers during air travel.

The issues surrounding incompleteness of data provided by airlines and also the lack of collaboration from airlines in providing airline manifests on request is of concern in this study and may have an impact on follow-up of other infectious diseases including those caused by emerging pathogens.

Conflict of interest

None declared.

Authors' contributions

The work presented here was carried out as a collaboration between all authors. All authors contributed to the collection and analysis of the data. PF and JOD defined the research theme. PF and JM analysed and interpreted the data. PF and JOD wrote the draft manuscript. All authors read and critically revised the first draft as well as subsequent drafts of this manuscript and approved the final version.

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Letter to the editor: Regarding the editorial by Penttinen and Friede

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To the editor: In the editorial by Penttinen and Friede, the authors summarised data from 2015 to 2016 on live attenuated influenza vaccine (LAIV) effectiveness in a Table and used the data in the Table to make several conclusions [1]. Unfortunately, the Table has several errors and, therefore, misrepresents the available data and studies. On 26 June 2016, the United States (US) Advisory Committee for Immunization Practices (ACIP) recommended that LAIV not be used during the 2016/17 season in the US [2]. Among all studies using a test-negative case–control design (TNCCD), the study from the US Centers for Disease Control and Prevention (CDC) (US Influenza Vaccine Effectiveness (VE) network) and the US Department of Defence (DoD) study (US Air Force School of Aerospace Medicine (USAFSAM) Sentinel Provider network) had the largest number of influenza A(H1N1)pdm09-infected children aged 2–17 years and larger or comparable numbers of children who received LAIV; these numbers were not correctly shown in the Table in the editorial. The US CDC study included 133 children aged 2–17 years who received LAIV (23 LAIV-vaccinated children had influenza A(H1N1)pdm09 infection) and 1,078 children who were unvaccinated. The US DoD study included 93 children vaccinated with LAIV (23 LAIV-vaccinated children had influenza A(H1N1)pdm09 infection) and 338 unvaccinated children (personal communication September 2016, Susan Federinko, USAFSAM). The youngest age for which LAIV is licensed for use in the US is two years; the US CDC VE estimates refer to children aged 2–17 years. The sample sizes for the other studies in the Table should also be consistently reported so that the same numerical comparisons are available for each study.

The authors incorrectly reported the lower confidence interval of the influenza A(H1N1)pdm09 VE estimate from the study in the United Kingdom (UK) as 8.5 instead of −8.5 [3]. They also incorrectly suggested in the text that this VE result was statistically significant, when it was not significant. Also, the VE estimate from Finland was for type A influenza, not for influenza A(H1N1pdm09). Thus, all studies that included an RT-PCR-confirmed H1N1pdm09 virus outcome failed to find statistically significant protection against influenza A(H1N1)pdm09 infection by LAIV. Conversely, all studies found significant protection against influenza A(H1N1)pdm09 infection for inactivated influenza vaccines (IIV) and reported higher point estimates for IIV [2,3]. In fact, US children who received LAIV were three times more likely to be influenza A(H1N1)pdm09 vaccine failures than children who received IIV during 2015/16 [2]. Data from the previous five influenza seasons in the US, and all other data from the US (ICICLE, DoD) and other countries that were available at that time, were used to inform the 26 June 2016 ACIP decision and the subsequent decision by the American Academy of Paediatrics [2,4,5]; both of these interim decisions are aimed at maximising the likelihood that influenza vaccination will protect US children in the upcoming season.

As Penttinen and Friede state, studies before the 2009 influenza pandemic suggested that LAIV was efficacious and offered some advantages over IIV in young children [1]. Also, some recent studies have suggested a role for LAIV in strategies to immunise against poorly immunogenic novel avian influenza viruses. Antibody titres after vaccination with either IIV or LAIV pre-pandemic avian influenza vaccines were suboptimal, even with higher antigen doses [6]. However, monovalent LAIV effectively primed for a protective antibody response to a single booster dose of IIV containing a matched or related haemagglutinin [6]. Thus, LAIVs have a role in strategies to prevent both seasonal and pandemic influenza infections. It is critical to understand why LAIV did not work as expected against the 2009 pandemic virus in the multivalent formations. In addition, information on the effects of prior vaccination on LAIV vaccine effectiveness will be critical since

US children have high influenza vaccine coverage and many are vaccinated with IIV before the age of two years. This information will improve future influenza LAIVs and enhance our ability to utilise them optimally.

Conflict of interest

None declared.

Authors' contributions

All authors contributed to the 600 words in the letter.

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Author's reply: Regarding the editorial by Penttinen and Friede

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To the editor: We thank Fry et al. for their interest in our editorial, in which we sought to lay out the evolving evidence surrounding the effectiveness of live attenuated influenza vaccine (LAIV) in preventing infections with influenza A(H1N1)pdm09 and the potential consequences of a perceived or true lack of effectiveness for childhood immunisation programmes and pandemic preparedness [1]. We appreciate that they meticulously highlight several errors in the Table and provided more accurate data which was not available to us through the original presentations from the United States (US) Advisory Committee on Immunization Practices (ACIP) [2]. All errors were corrected in the original text on 29 September and the more accurate sample sizes and confidence intervals were incorporated as suggested. In our view, these amendments do not change our conclusions. We look forward to the peer-reviewed publication of vaccine effectiveness (VE) studies done in the US as important contributions to the evidence base.

Fry et al. note that the VE estimate for Finland referred to all type A influenza, not specifically to influenza A(H1N1)pdm09. However, it is important to note that only 7% of subtyped influenza viruses during the 2015/16 season from Finland were influenza A(H3N2), and almost all of those came from adult patients [3]. Therefore, we assume that the VE estimate against influenza A in Finland accurately reflects the VE against influenza A(H1N1)pdm09 in children.

We note that Fry et al. agree with our final conclusion in that 'It is critical to understand why LAIV did not work as expected against the 2009 pandemic virus in the multivalent formulations' [4]. We suggest that the international scientific collaboration already established between the involved public health agencies under the coordination of the World Health Organization continues at an intensive pace in order to ensure that the scientific community, the public health community, policymakers and manufacturers resolve this critical question..

Conflict of interest

None declared.

Authors' contributions

Both authors contributed equally to conception and writing of this letter.

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